

Evidence-based Practice Center Technical Brief Protocol

Project Title: Medication-Assisted Treatment Models of Care for Opioid Use Disorder

I. Background and Objectives for the Technical Brief

Opioid use disorder (OUD) has been identified by the Department of Health & Human Services as a national crisis.¹ OUD involves misuse or abuse of prescription opioids or illicit heroin, and is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)² as “a problematic pattern of opioid use leading to clinically significant impairment or distress.” In 2014, approximately 1.9 million Americans 12 years or older were estimated to have OUD due to prescription drugs and nearly 600,000 due to heroin use.³ OUD is associated with decreased quality of life and increased morbidity and mortality. In 2013, an estimated 16,000 individuals died as a result of prescription opioid overdose (a 2.5-fold increase from 2001) and approximately 8,000 from heroin (a 4-fold increase from 2001).⁴ These trends have occurred in conjunction with markedly increased rates of opioid prescribing for chronic pain;⁵⁻⁹ in fact, the majority of heroin users now report that their first opioid of abuse was a prescribed opioid, not heroin.¹⁰ Challenges in the treatment of OUD include the relapsing nature of this condition, the frequent presence of psychological and medical comorbidities, and the disproportionate impact on those in socioeconomically disadvantaged settings with limited access to care.^{11,12} Compared with OUD due to prescription drugs, OUD related to heroin is associated with additional risks from the high addiction potential of heroin, lack of control over drug purity, and possibility of blood-borne disease transmission (stemming from injection behaviors commonly used to take heroin).

As noted in 1997 by a National Institutes of Health consensus panel, opioid addiction “is a medical disorder that can be effectively treated with significant benefits for the patient and society.”¹³ Medication-Assisted Treatment (MAT) is a multi-component approach to treatment of OUD that combines use of opioid agonists, partial agonists, or antagonists that are approved by the U.S. Food and Drug Administration (FDA) for treatment of this condition accompanied by various psychosocial interventions.¹⁴ MAT has been shown to be more effective than detoxification and abstinence in reducing the frequency and quantity of opioid use as well as the risk of overdose, improving social functioning, and decreasing criminal activity and disease rates. Treatment programs that include both the medication and psychosocial components are more effective than programs without both types of interventions and are associated with better treatment retention.¹⁵ The purpose of the medication component is to block the euphoric and sedating effects of other opioids, reduce the craving for other opioids, and/or mitigate the symptoms of opioid withdrawal. Psychosocial interventions address the psychosocial contributors to addiction and include strategies such as individual therapy, group counseling, family behavior therapy, cognitive-behavioral therapy, and assessment and

coordination of other medical and psychiatric needs such as other substances of abuse, human immunodeficiency virus (HIV) or hepatitis C virus (HCV) co-infection, or pregnancy.¹⁵

Current Practices

The White House and the Department of Health & Human Services recently identified improving access to MAT as a key priority for reducing harms associated with OUD.^{1,16} Prior to the Drug Abuse Treatment Act (DATA) of 2000, MAT could only be provided through federally-approved opioid treatment programs.¹⁷ DATA 2000 permits physicians to obtain a waiver and prescribe the partial opioid agonist buprenorphine (co-formulated with the antagonist naloxone) for OUD. Although this has increased access to buprenorphine in primary care settings, research indicates that access to and use of MAT remains limited.^{4,18} In many rural areas, for example, no MAT prescribers are available.¹⁹ Even in specialty addiction treatment settings, medications approved for MAT appear to be underutilized, with one study showing that MAT was used in only about one-third of patients.²⁰ Therefore, understanding the most effective and promising models of care and implementation strategies are critical for optimizing the impact of initiatives to expand access to MAT.¹

Objective of Technical Brief

The purpose of this Technical Brief is to describe the available literature on MAT models of care and methods for effective MAT implementation, and to identify and summarize key issues and gaps in the evidence base. A Technical Brief does not synthesize data on outcomes or grade evidence. Rather, it seeks to summarize the state of the science, provide a conceptual or organizational framework to understand key components of the intervention of interest, highlight promising new and innovative strategies, describe barriers to implementation, and provide guidance regarding future research directions and priorities. The Technical Brief will focus on implementation of MAT in primary care settings, including rural or other underserved settings. Specifically, Guiding Question 1 provides a descriptive overview of MAT, Guiding Question 2 describes the context in which MAT is implemented, Guiding Question 3 summarizes the current state of the evidence of MAT, and Guiding Question 4 addresses important issues and future directions for MAT. This technical brief is intended to help determine the scope of future research, such as a subsequent systematic evidence review on MAT.

II. Guiding Questions

1. *Description/Overview of MAT for the Treatment of Opioid Use Disorder:*
 - a. What are the different types or models of care of MAT that have been proposed or used in clinical practice?
 - b. What are the potential advantages and disadvantages, of these respective models of care?
2. *Context in Which MAT is Used:*
 - a. In what settings is MAT currently implemented?

- b. Are there special considerations for implementing MAT in primary care, including rural or other underserved settings?
 - c. What are potential barriers to implementation, including resources needed, and how do barriers vary according to the setting?
 - d. What kinds of training, certification, and staffing are required for various MAT models of care?
3. *Current Evidence on MAT:*
- a. What have published and unpublished studies reported on the use of and effectiveness MAT in primary care settings, including rural or other underserved settings? The technical brief will summarize the following information:
 - i. Patient population, including practice setting and country/location
 - ii. Details on MAT model of care, including the types of interventions used (specifics of pharmacological and nonpharmacological treatments), provider type/staffing needs, implementation strategy/mode of delivery, frequency, and other factors
 - iii. Study design/size
 - iv. Comparator used in comparative studies
 - v. Concurrent/prior treatments
 - vi. Length of followup
 - vii. Outcomes measured
 - viii. Adverse events/harms/safety issues reported
4. *Important Issues and Future Directions for MAT:*
- a. What are promising new and innovative strategies in MAT models of care?
 - b. Given the current state of the evidence, what are the implications for the current level of diffusion and/or further diffusion of MAT?
 - c. What are the ethical, privacy, equity, cost, and/or economic efficiency considerations that impact diffusion, decision-making, and/or conceptual thinking around MAT?
 - d. What are important areas of uncertainty for MAT?
 - e. What are possible key areas of future research on MAT, and what areas related to MAT warrant a systematic review?

III. Methods

The Technical Brief will integrate discussions with Key Informants with searches of the published literature and grey literature to inform the above Guiding Questions.

1. Data Collection:

A. Discussions with Key Informants

We will identify Key Informants that represent broad and balanced perspectives relevant to MAT, particularly with expertise or experience related to implementation in primary care settings, including rural or other underserved settings. Key Informants will include a concise group (≤ 9) of researchers, clinicians, and representatives from health policy and implementation arenas, professional societies and organizations, and patient groups, and additional federal representatives.

We will organize and facilitate phone discussions with the Key Informants to gain input on the Guiding Questions, which will be conducted in small groups (3 to 4 Key Informants) to maximize efficiency and allow all representatives the chance to provide input. Members of our research team and the AHRQ Task Order Officers will also attend the calls. On the calls, the Key Informants will be engaged using a semi-structured approach. They will be asked to respond to pre-determined questions targeted to the specific Key Informant perspectives, share more general insights, and interact with each other. The questions will be used as a guide, but we may ask additional or supplemental questions depending on the direction of the interviews and their responses. We will ask which MAT models of care are in use in primary care and other related settings, including models of care which are not described in the published literature, and will look for insights into what components are working, the current challenges or barriers to implementation, patient preferences, and future directions, including promising new and innovative models and strategies for implementation. We will also ask about specific issues to be aware of when reviewing the literature, such as outcomes to be prioritized, meaningful length of followup, study design issues, and how MAT models of care vary in terms of intensity, goals, and components of care. We are particularly interested in asking about the feasibility and applicability of models of care implemented in one setting or population to others and about identifying models of care that may be particularly suitable for specific settings, including rural and other underserved settings. Specific sample questions to be asked of the Key Informants based on perspective are listed below in **Table 1**. The calls will be recorded, and the key points will be summarized and shared with the group. We will review all of the Key Informant input regarding successful and promising MAT models of care and develop a framework for categorizing the different types of components in MAT models of care, to help organize and provide a structure for future research and discussions around this area. The feedback from the Key Informants will be integrated with the expertise of our project team and the evidence that we identify through the published and unpublished literature.

Table 1. Sample Questions for Key Informants

Key Informant Perspective	Sample Questions
Researchers and Clinicians (including Professional Societies and Organizations)	<p>Guiding Questions 1, 2, and 4.</p> <p>In addition:</p> <ol style="list-style-type: none"> 1. What outcomes should be prioritized? 2. In your experience, what MAT models of care have been particularly successful and why? 3. Are there models of care that are particularly suited (e.g., feasibility, applicability) for rural or other underserved settings? 4. How would you categorize the components of MAT models of care? 5. What MAT models of care components are most critical for effectiveness? 6. What are barriers to implementation of MAT in primary care settings? 7. What are specific barriers to implementation of community-based psychosocial programs in MAT? 8. How could barriers to implementation be overcome? 9. Are you aware of new or innovative models of care that warrant additional research? 10. What are key research needs to understand effectiveness and implementation of MAT models of care? 11. What types of study designs would be useful for studying new or innovative MAT models of care? 12. What is a meaningful length of follow-up? 13. Are there specific areas related to effectiveness or implementation of MAT models of care that have been sufficiently studied to warrant a systematic evidence review?
Health Policy and Implementation Arenas	<ol style="list-style-type: none"> 1. What outcomes of MAT are important from a health policy/payer perspective? 2. What policies do payers put in place to influence use of MAT for treatment of opioid use disorder? 3. How are decisions to cover or implement MAT made at a policy level or at an institutional/clinical setting level? 4. What are some research questions about MAT that you would like answered to inform policy and implementation decisions? 5. Are you considering new policies to improve the use of MAT, particularly in primary care, including rural or other underserved populations? 6. What are cost and/or economic efficiency considerations that impact diffusion, decision-making, and/or conceptual thinking around MAT?
Patient Perspective	<ol style="list-style-type: none"> 1. What values do patients place on various non-substance-use-related outcomes and how do patients weigh trade-offs related to different pharmacological and non-pharmacological approaches? 2. What factors or themes are most important to patients receiving MAT? 3. What components of MAT are important for patients to know, that they may not be aware of? 4. What common experiences do patients in MAT programs describe? 5. Should the use of MAT programs be expanded; and if so, what settings for patients are most amenable to the implementation of MAT? 6. What barriers do patients experience in obtaining MAT? 7. What suggestions do patients have for improving MAT models of care? 8. What are ethical, privacy, equity, or cost considerations that impact patient's use of MAT?

MAT = medication-assisted treatment

B. Grey Literature search

To identify grey literature, the Agency for Healthcare Research and Quality's (AHRQ) Evidence-based Practice Center (EPC) Scientific Resource Center (SRC) will send email notification to relevant stakeholders about the opportunity to submit Scientific Information Packets (SIP) via the Effective Health Care (EHC) web site.

Source: www.effectivehealthcare.ahrq.gov

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In addition, we will conduct searches of the grey literature, which will be identified using suggestions from our Key Informants, as well as Internet searches. We will search ClinicalTrials.gov and Health Services Research Projects in Progress (HSRProj) for ongoing research, as well as Google Scholar, NIH Reporter, and web sites of government agencies with MAT initiatives. The grey literature searches will be used to primarily inform Guiding Question 3, but if information relevant to the other Guiding Questions is identified, it will also be discussed in the report.

C. Published Literature search

We will search, review, and summarize the available literature to address Guiding Question 3 on the efficacy and safety of MAT for OUD in primary care settings. To identify published articles for this review, an experienced research librarian will create search strategies of search terms and medical subject headings (MeSH) for the following databases: Ovid Medline, PsycINFO, the Cochrane Library, SocINDEX, and CINAHL. A sample search strategy is listed below in **Table 2**. The search will also provide a background to inform the Key Informant input obtained for Guiding Questions 1, 2, and 4. We restricted the searches to start in 1995, as addiction could not be treated with MAT in the primary care/non-addiction treatment settings until the year 2000, following the passage of the Drug Addiction Treatment Act (DATA).

Table 2. Sample Search Strategy

1. Opiate Substitution Treatment/
2. exp Opioid-Related Disorders/dt, pc, px, rh, th
3. methadone.mp. or exp Methadone/
4. buprenorphine.mp. or Buprenorphine/
5. naltrexone.mp. or Naltrexone/
6. medication-assisted treatment.mp.
7. medication assisted treatment.mp.
8. ((opiate* or opioid* or oxycodone or hydrocodone or hydromorphone or heroin or morphine) adj2 (substitut* or replace* or maintenance) adj2 (treatment* or therap*)).ti,ab.
9. ((opiate* or opioid* or narcotic* or oxycodone or hydrocodone or hydromorphone or heroin or morphine) adj2 (misuse or abuse or disorder* or addition* or dependence)).ti,ab.
10. 3 or 4 or 5
11. 9 and 10
12. 1 or 2 or 6 or 7 or 8 or 11
13. limit 12 to humans
14. limit 13 to English language

We will also review the reference lists of identified publications and add any previously unidentified papers. In addition, we will update the searches while the report is undergoing peer and public review in order to capture any recently added publications. If any new studies are identified from the update searches or arise as suggestions from the peer or public review, they will be added to the report prior to finalization of the report.

Working from this evidence base, we will apply well-defined screening criteria and use efficient title and abstract review processes to identify the most relevant and authoritative evidence on MAT models of care in primary care settings, implementation strategies, particularly in primary care and rural settings, and will also highlight contextual factors, such as the setting (e.g., urban vs. rural), patient characteristics (e.g., age, comorbid conditions, opioid use disorder related to prescription opioid use for chronic pain versus unprescribed opioid use), and intervention characteristics (e.g., components of MAT models of care, degree of coordination, intensity of treatment), that may affect the application of MAT models of care. We will summarize findings from high-quality systematic reviews, such as six Cochrane reviews on MAT,²¹⁻²⁶ including limitations of the evidence (e.g., the Cochrane reviews focus solely on the effects of the medication component of MAT in specialty treatment centers).

All titles and abstracts identified through searches will be independently reviewed for eligibility against our inclusion/exclusion criteria organized by PICOTS (population, intervention, comparator, outcome, timing, study design) (**Table 3**) by a trained member of the research team. Studies marked for possible inclusion by any reviewer will undergo a full-text review. For abstracts without adequate information to determine inclusion or exclusion, we will retrieve the full text and then make the determination. All results will be tracked in an EndNote® database (Thomson Reuters, New York, NY). Each full-text article will be independently reviewed by two trained members of the research team for inclusion or exclusion on the basis of the eligibility criteria. If the reviewers disagree, conflicts will be resolved by discussion and consensus or by consulting another member of the review team. Results of the full text review will also be tracked in the EndNote® database, including the reason for exclusion for excluded full-text publications when they did not meet the eligibility criteria.

Table 3. Draft Inclusion and Exclusion Criteria for Guiding Question 3 on the Efficacy and Safety of MAT

PICOT	Include	Exclude
Populations	Patients with OUD in primary care settings, including rural or other underserved settings	MAT in inpatient settings and licensed treatment centers
Interventions	MAT programs for OUD	--
Comparators	Will include studies of MAT models of care without a comparator, as well as studies that compare MAT models of care with one another	--
Outcomes	Measures of use or access Substance-use-related outcomes, including mortality, overdose, substance use Non-substance-use-related outcomes, including quality of life, functional status, work status, engagement in criminal activity, rates of unplanned pregnancy, acquisition or transmission of infectious conditions, and others; in pregnant women, maternal and fetal health outcomes	--
Timing	Any	--
Study Design	Systematic reviews Randomized controlled trials Observational studies, including cohort studies, case control studies, and other experimental and non-experimental study designs	Non-systematic reviews Studies without original data Non-English language Non-human

MAT = Medication-Assisted Treatment; OUD = opioid use disorder; PICOTS = population, intervention, comparator, outcome, timing, study design

2. Data Organization and Presentation:

For studies meeting inclusion criteria, we will design data abstraction forms to summarize pertinent information from each study, such as characteristics of study populations, interventions, comparators, outcomes, study designs, settings, and methods. All data abstractions will be reviewed for completeness and accuracy by another member of the team.

A. Information Management

Data from the published literature will be integrated with information from the gray literature and discussions with Key Informants. Data elements to be abstracted into evidence tables are listed in **Table 4**, which will be used to address the Guiding Questions, particularly Guiding Question 3, and also develop a conceptual framework for the existing evidence on MAT.

Table 4. Proposed Data Elements to be Abstracted into Evidence Tables for Each Study for Guiding Question 3

Data Element	Details
Study characteristics	Study design Inclusion/exclusion criteria Sample size at recruitment and followup rates
Population characteristics	Age (mean, range) Race (percentages) Other characteristics relevant for MAT for OUD, including duration of treatment, other substances used, co-morbidities (e.g., HIV, HCV), etc.
Intervention characteristics	Description of MAT program/model of care including the types of interventions used (specifics of pharmacological and nonpharmacological treatments), provider type/staffing, implementation strategy/mode of delivery, frequency, and other factors.
Comparator	Comparator(s), if any
Outcomes examined	Types of outcomes examined in the study and how they were measured, and main findings
Timing	Timing of outcome measurement (follow-up)
Setting	Setting of where MAT was implemented and managed Country/geographic location

HCV = hepatitis C virus; HIV = human immunodeficiency virus; MAT = Medication-Assisted Treatment; OUD = opioid use disorder

B. Data Presentation

We will present our findings in the order of the Guiding Questions. We will categorize and summarize findings from the grey literature and the Key Informant interviews qualitatively in the text of the report. For Guiding Questions that have empirical evidence, primarily Guiding Question 3, we will present our findings in tables that describe the state of the evidence as outlined above, and summarize the findings in the text of the report.

If amenable, we will also present some of the findings graphically to visually represent the state of the science of MAT for OUD.

IV. References

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V. Definition of Terms

Not applicable.

VI. Summary of Protocol Amendments

No amendments have been made to the current version of this protocol.

VII. Key Informants

Within the Technical Brief process, Key Informants serve as a resource to offer insight into the clinical context of the technology/intervention, how it works, how it is currently used or might be used, and which features may be important from a patient or policy standpoint. They may include clinical experts, patients, manufacturers, researchers, payers, or other perspectives, depending on the technology/intervention in question. Differing viewpoints are expected, and all statements are crosschecked against available literature and statements from other Key Informants. Information gained from Key Informant interviews is identified as such in the report. Key Informants do not do analysis of any kind nor contribute to the writing of the report and have not reviewed the report, except as given the opportunity to do so through the public review mechanism.

Key Informants must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

VIII. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodologic expertise. Peer review comments on the preliminary draft of the report are considered by the EPC in preparation of the final draft of the report. Peer reviewers do not participate in writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual reviewers. The dispositions of the peer review comments are documented and will be published three months after the publication of the Evidence report.

Potential Reviewers must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than \$10,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

IX. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than \$1,000 and any other relevant business or professional conflicts of interest.

Related financial conflicts of interest that cumulatively total greater than \$1,000 will usually disqualify EPC core team investigators.

X. Role of the Funder

This project was funded under Contract No. HHSA290201500009I from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The Task Order Officer reviewed contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.